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(54) Title: PROCESS FOR PRODUCING NITROSONIUM IONS			
(57) Abstract			
<p>A process for producing nitrosonium ions is described, in which a nitroxyl compound such as TEMPO is oxidised using an oxidising agent in the presence of a complex of a transition metal such as Mn, Fe, Cu, and a complexing agent such as a polyamine. The process is useful for the oxidation of carbohydrates containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 100 or per 25 monosaccharide units and per molecule.</p>			

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PROCESS FOR PRODUCING NITROSONIUM IONS

- [0001] The invention relates to the production of nitrosonium ions (oxoammonium ions) by oxidation of nitroxyl radicals, especially 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO). The nitrosonium ions can be used as a catalytic oxidising agent for the selective oxidation of primary alcohols to aldehydes.
- [0002] Such a process in which TEMPO is reoxidised by chemical means is known from a review by De Nooy in *Synthesis* 1996, 1153-1174 and from WO 95/07303.
- [0003] It was found according to the invention that oxidation of alcohol functions, especially primary alcohol functions, using nitrosonium ions, can be carried out without using chlorine-based oxidising agents and with the use of hydrogen peroxide or oxygen as the ultimate oxidising agent. The oxidation according to the invention is performed using transition complexes of a transition metal and a complexing agent as intermediate oxidants. This oxidation, when carried out on primary alcohols, results in the formation of aldehydes.
- [0004] The aldehydes may be present in the (hemi)acetal form and related structures. The process is particularly suitable for oxidising carbohydrates having primary alcohol functions. An adaptation of the oxidation of the invention can be used to oxidise secondary alcohols, especially carbohydrates, to keto derivatives. The process of the invention is further defined by the characterising features of the appending claims.
- [0005] In the following description, reference is made to TEMPO only for the sake of simplicity, but it should be understood that other suitable nitroxyls, i.e. organic nitroxyl compounds lacking α -hydrogen atoms, such as 2,2,5,5-tetramethylpyrrolidine-N-oxyl (PROXYL), 4-hydroxy-TEMPO, 4-acetamido-TEMPO and derivatives thereof and those described in WO 95/07303 can be substituted for TEMPO. These di-tert-alkyl nitroxyls are especially suitable for selectively oxidising primary alcohols to aldehyde functions, in particular in the presence of secondary alcohol functions that should not be oxidised. Less sterically hindered nitroxyls, such as 4,4-dimethyloxazolidine-N-oxyl (DOXYL), are suitable for preferentially oxidising secondary alcohols to keto functions, for example in the production of keto starch. The active oxidising species is the nitrosonium ion (oxoammonium ion $>\text{N}^+=\text{O}$), that is produced in situ by oxidation of the corresponding hydroxylamine and nitroxyl radical. If desired, the reaction can be performed in two steps, the production of the nitrosonium ion being the first and the oxidation of the alcohol function being the second.
- [0006] A catalytic amount of nitroxyl is preferably 0.1-25 % by weight, based on the primary alcohol, or 0.1-25 mol% with respect to the primary alcohol. The nitroxyl may also be immobilised, e.g. by coupling of the hydroxyl group of 4-hydroxy-TEMPO to a suitable

carrier, or in the form of a polymeric nitroxyl such as:

-[(CH₃)₂C-NO.-C(CH₃)₂-A-]_n, wherein A may be an alkylene group and/or a heteroatom, and n is a number from e.g. 10 up to several hundreds.

[0006] The process of the invention results in oxidation of primary alcohols initially to the corresponding aldehydes. If required the primary products can be further oxidised to the corresponding carboxylic acids by using known oxidising agents such as hypochlorite, chlorite, hydrogen peroxide or by using TEMPO-mediated oxidation under more vigorous conditions such as an increased temperature e.g. from 40-80 °C, or for prolonged exposure to the reaction conditions. Alternatively, the aldehyde/carboxylic acid ratio can be increased by using relative low pH's (e.g. pH 3-7), by controlled addition of oxidising agent, by lowering the oxygen concentration, or by first preparing the nitrosonium ion solution (two-step process).

[0007] The present process is especially favourable for the selective oxidation of primary hydroxyl groups in alcohols having a secondary alcohol function in addition to the primary alcohol, such as 1,6-octanediol, 1,9-octadecanediol, steroid hormones, sugar alcohols, glycosides (flavour precursors), and in particular carbohydrates having primary alcohol functions. The carbohydrates may be monosaccharides, such as glucose, fructose, disaccharides, such as sucrose, maltose, lactose, oligosaccharides and polysaccharides. The oligo- and polysaccharides may be of any type, e.g. glucans such as starch, starch components (i.e. amylose, amylopectin, dextrans), pullulan (α -1,4- α -1,4- α -1,6-glucan), chitin, lichenin etc., furanofructans such as inulin and levan, galactans, arabinogalactans, furanoid pentosans (xylans), (galacto)mannans (guar, locust bean gum), bacterial exopolysaccharides (EPS) and the like and derivatives of such carbohydrates, such as hydrolysates. These oligo- and polysaccharides include heterosaccharides, i.e. those which have different structural units, even if those different units themselves may not have primary hydroxyl groups such as uronic acid units, e.g. in xanthan and carbohydrates derived from algae. The carbohydrates to be oxidised according to the invention include glycosides and other protected carbohydrates. Further examples are glyconic acids, such as lactobionic acid delta-lactone, that can be oxidised to glycaric acids and the like.

[0008] A distinct group of compounds suitable for oxidation with the present process consists of hydroxyalkylated carbohydrates such as hydroxypropyl starch or hydroxyethyl inulin, which result in an alternative way for producing formylalkyl carbohydrates. Other suitable carbohydrate substrates in which at least a part of the (6-) hydroxymethyl groups are intact, include for example (2- and 3-) carboxymethyl carbohydrates.

[0009] The oxidation of carbohydrates containing primary hydroxyl groups results in the corresponding carbohydrates containing aldehydes and, if desired, to carboxylic acids, with

intact ring systems. Examples include α -1,4-glucan-6-aldehydes, β -1,4-glucan-6-aldehydes, β -2,1-fructan-6-aldehydes and β -2,6-fructan-1-aldehydes. These products are useful intermediates for functional carbohydrates wherein the aldehyde groups are further reacted with e.g. amine compounds and the like. They are also useful intermediates for crosslinked carbohydrates, in which the aldehyde groups are further reacted with e.g. diamine reagents.

[0010] The catalysts to be used according to the invention are complexes of transition metals, i.e. coordination compounds between a transition metal and an organic molecule as a complexing agent having one or more free electron pairs, especially nitrogen compounds.

10 Suitable nitrogen compounds include amino acids, phenanthrolines and other polyamines. A polyamine, which forms a complex with the transition metal, is understood to refer to compounds which comprise at least two amine nitrogen atoms, separated by at least two carbon atoms. Preferably, the polyamines comprise at least three nitrogen atoms which in each case are separated by two or more, in particular two or three, more in particular two, carbon atoms. The remaining valencies of the nitrogen atoms are preferably bound with small alkyl groups, in particular methyl. It is also possible for the polyamines to have ether or alcohol functions. The polyamines can be linear or cyclic. The polyamines should be alkaline, i.e. should not contain acid functions. Examples of polyamines which can be employed are 2,2'-bipyridyl, 2,2'-bipyrrole, 2-(dimethylaminomethyl)pyridine, tetramethylethylenediamine, pentamethyldiethylenetriamine, 1,4-dimethylpiperazine, 1,4,7-trimethyl-1,4,7-triaazonane (= triazacyclononane), 1,4,7-trimethyl-1,4,7-triazecane, 1,4,7,10-tetramethyl-1,4,7,10-tetraazacyclododecane, 1,2-bis(4-methyl-1-piperazinyl)-ethane, 1,2-bis(4,7-dimethyl-1,4,7-triaazonan-1-yl)ethane, and the corresponding compounds wherein one or more of the said methyl groups have been replaced by, for example, ethyl groups. It is also possible to use porphin and other porphyrins and corresponding macrocyclic polyamine compounds. Histidine and comparable amino acids having an additional nitrogen atom, and their oligopeptides such as histidyl-histidine, are other examples of suitable complexing agents. Preference is given to compounds of the bipyridyl type, triazonane type and to amines whose remaining valencies are linked to methyl groups. The counterions required for neutrality of the complexes may be common, preferably non-toxic counterions such as oxide, halide, perchlorate, acetylacetone, nitrate, sulphate and the like.

[0011] Transition metals to be used in the metal complexes include especially those of the fourth period of the periodic table of elements from vanadium to zinc, preferably manganese, iron, cobalt, nickel and copper, in particular manganese, iron, cobalt and copper. The corresponding metals from the higher periods may also be used, such as in

particular ruthenium. The metal complexes require hydrogen peroxide, alkyl and ar(alk)yl hydroperoxides (such as tert-butyl hydroperoxide), oxygen or chlorite as an ultimate electron acceptor. About one metal atom to two to four nitrogen atoms of the complexing agent can suitably be used.

5 [0012] The metal complex may be used in a catalytic amount, e.g. in about an equimolar amount with respect to the nitroxyl compound. Suitable amounts of metal complexes are for example 1-25 mol% with respect to the alcohol to be oxidised.

[0013] The process of the invention can be performed under relatively mild conditions, e.g. at a pH between 5 and 10, and at a temperature between 15 and 60°C (both depending 10 on the particular metal complex). The reaction medium can be an aqueous medium, or a homogeneous mixed medium, e.g. of a mixture of water and a secondary or tertiary alcohol or an ether/water mixture, or a heterogeneous medium, e.g. a mixture of water and a water-immiscible organic solvent such as a hydrophobic ether, a hydrocarbon or a halogenated hydrocarbon. In the latter case, the metal complex and/or the nitroxyl and the oxidising 15 agent may be present in the aqueous phase and the alcohol substrate and the aldehyde or ketone product may be present in the organic phase. If necessary, a phase transfer catalyst may be used. The reaction medium can also be a solid/liquid mixture, in particular when the nitroxyl is immobilised on a solid carrier. A heterogeneous reaction medium may be advantageous when the substrate or the product is relatively sensitive or when separation of 20 the product from the other reagents may present difficulties.

[0014] The invention also pertains to novel carbohydrate oxidation products and derivatives thereof, which can be obtained with the process of the invention. These include polysaccharides in which at least 1 hydroxymethyl per 100, especially per 50 or even per 25, monosaccharide units has been converted to a carbaldehyde group, whether or not in 25 hemiacetal or similar form, with the proviso that on average each molecule contains at least 1 carbaldehyde group other than a possible (hemiacetalised) aldehyde group at the reducing end of an oligo- or polysaccharide. When the carbohydrate is starch, the degree of oxidation is at least one carbaldehyde group per 25 anhydroglucose units. The carbaldehyde group is preferably present in chain (backbone) units, rather than in branch or 30 terminal units. The novel products include glycoside derivatives, i.e. products which, in addition to an acetalised end group have at least one carbaldehyde group obtainable by oxidation of non-galactose hydroxymethylene groups. In the products of the invention, the monosaccharide rings that carry the carbaldehyde group are largely intact. The only common carbohydrate derivatives having a predominant content of aldehyde groups are 35 periodate-type oxidation products of starch, cellulose and the like, in which the rings bearing the aldehyde groups are broken. The aldehyde carbohydrates covered by the

present invention are especially of types other than the cellulose or pentosan type (or derivatives such as carboxymethylated, alkylated, hydroxyalkylated cellulose). The products obtainable according to the invention may contain, in addition to the aldehyde groups, other functional groups, especially carboxyl groups obtained by further oxidation or by carboxyalkylation.

5 [0015] The novel derivatives of the invention are very suitable as thickeners, viscosifiers, stabilisers, wet strength additives, water-absorbing polymers and the like, and especially as starting materials for further functionalisation, especially with alcohols, amines, and other agents capable of coupling with an aldehyde function. Such agents include crosslinking 10 agents (diamines, diols and the like), which can be used to crosslink the carbohydrates or to couple them to amino acids, proteins, active groups etc.

[0016] The process of the invention can also advantageously be used for modifying biopolymers such as starch, non-wood cellulose to allow derivatisation or to adapt viscosity and other physical or chemical properties such as (textile) strength, dyeability, etc.

15 [0017] The invention also pertains to derivatives obtained by coupling of the aldehyde carbohydrates described above with e.g. amines, especially by reductive amination, to produce imino or amino derivatives of carbohydrates as defined in the appending claims. Also, the aldehyde carbohydrates can be reacted acetalised with hydroxy-functionalised compounds, e.g. glycolic acid, for further derivatisation.

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Examples: General

[0018] Uronic acid (6-COOH of hexopyranose units) contents were determined using the Blumenkrantz et al. method (*Anal. Biochem.* (1973) 54, 484), using boric acid (0.0125 M) in concentrated sulphuric acid, adding 3-hydroxybiphenyl and measuring the 25 extinction at 520 nm.

[0019] Aldehyde contents were determined either by a subtractive method (determining the uronic acid content before and after of oxidation of aldehydes with chlorite and hydrogen peroxide), or by addition of hydroxylamine hydrochloride to produce an oxime and back-titration of liberated hydrochloric acid, or by ¹³C NMR 30 spectroscopy (intensity of C6 signal of aldehyde with respect to C1 of anhydroglucose unit, or intensity of C6 (C=N) in the oxime).

Example 1: C6 Oxidation of methylglucopyranoside with TEMPO / Mn / hydrogen peroxide

35 [0020] Sixty mg of α -methylglucopyranoside, 30 mg of Mn complex with 1,4,7-trimethyl-1,4,7-triazonane and 500 mg TEMPO (lower amounts work equally well) were

dissolved in 100 ml of demineralised water. The reaction temperature was raised to 55-60°C and the pH was maintained at 8.5. Diluted hydrogen peroxide (31 µl 30% in 10 ml demineralised water) was added over 5 h. After overnight reaction, the C6 carboxyl and C6 aldehyde contents were qualitatively shown using DIONEX HPAEC. A sample was 5 reduced with sodium borohydride at pH 8 to confirm the presence of aldehyde functions. The carboxyl content was determined using the Blumenkrantz method to be 20%. After further oxidation of aldehyde (hemiacetal) with sodium chlorite and hydrogen peroxide, the carboxyl content was 26%. Thus the aldehyde content was 6%.

10 **Example 2: Oxidation of methylglucopyranoside with TEMPO / Mn / hydrogen peroxide [0021]** To an aqueous solution of 500 mg methylglucopyranoside and 250 mg manganese (II) nitrate, 10 ml 0.05 M bipyridyl solution and 50 mg TEMPO, 0.70 ml hydrogen peroxide (3 % w/w) is added in portions of 20 µl in the course of 8 h. The pH of the mixture is kept between 6 and 7. The next day the mixture is treated with sodium 15 chlorite to convert the aldehyde groups to carboxylic acid groups. (pH 4-5). The yield of uronic acid before and after further oxidation is 8 and 11 %, respectively.

Example 3: C6 Oxidation of methylglucopyranoside with TEMPO / Cu / oxygen [0022] Sixty mg of α-methylglucopyranoside, 500 mg TEMPO and 24 mg copper / 20 histidine complex were dissolved in 100 ml of demineralised water. The reaction temperature was maintained at 30°C and the pH was adjusted to 8.0. Oxygen was passed through the solution for two hours. After overnight reaction, the carboxyl content was determined using the Blumenkrantz method and found to be 17%.

25 **Example 4: Oxidation of pullulan by TEMPO / Mn / H₂O₂ [0023]** In 50 ml of water 400 mg pullulan (2.4 mmol anhydroglucose units) and 50 mg of TEMPO were dissolved. To this solution 50 mg manganese nitrate and 5 ml bipyridine 0.05 M solution were added, followed by small amounts of hydrogen peroxide. (100 µl 3% w/v per time). The pH was maintained between 6.5 and 7.0. In 30 total 2.0 ml hydrogen peroxide (3%) was added. After one day the aldehyde groups present were converted to carboxylic acid groups by reaction with sodium chlorite/hydrogen peroxide (pH 4-5). The yield of uronic acid with respect to groups was 25%.

35 **Example 5: Oxidation of pullulan by TEMPO / Mn / H₂O₂ [0024]** In 25 ml of water 250 mg pullulan and 20 mg of TEMPO were dissolved. To

this solution 25 mg manganese nitrate was added, followed by 100 µl of hydrogen peroxide (3% solution, w/w) and bipyridine solution (5 ml 0.05 M). The reaction was conducted at pH 6.5. At the first day 60 mg (1.8 mmol) hydrogen peroxide was added and after one day 25 mg of uronic acid was formed. During the second day 30 mg hydrogen peroxide was added and the amount of uronic acid was increased to 50 mg. The aldehyde groups were converted into carboxylic acid groups with hydrogen peroxide/sodium chlorite the content raised to 90 mg. (D.O. 60%). This example shows that higher levels of oxidising agent and longer reaction times lead to higher yields, compared to example 4.

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Example 6: Oxidation of pullulan with TEMPO / Mn / oxygen

[0025] To a solution of 400 mg pullulan in 25 ml water 50 mg TEMPO, 180 mg manganese nitrate and 10 ml 0.05 M bipyridine were added. The pH was brought to 9 and oxygen gas was bubbled through the solution. A fast decrease in pH was observed. 15 By addition of sodium hydroxide the pH of the solution was kept at 9. After one night of reaction the uronic acid content of the reaction mixture was determined according to the Blumenkrantz method 20 % of uronic acid was formed.

Example 7: Oxidation of α -methylglucopyranoside with hydrogen peroxide, cobalt chloride (II) and bipyridine.

[0026] To a solution of 80 mg α -methylglucopyranoside and 25 mg TEMPO in 5 ml water, 2 ml of a 0.08M cobalt(II) chloride solution and 4 ml bipyridine solution were added. After adjusting the pH by addition of 0.05 M NaOH to 7, 50 ml hydrogen peroxide solution (3% w/w) was added. This resulted in a pH drop followed (usually after 10 to 15 minutes) by an increase When the pH was at its original value again, 50 ml hydrogen peroxide was added. In total 350 ml was added. After standing for one night the pH was brought to 3.5 and 100ml hydrogen peroxide (30% w/w) and 100 mg sodium chlorite (Aldrich 80% purity) were added. After reacting for two hours the uronic acid content was determined. According to the Blumenkrantz method, before subsequent oxidation 9% and thereafter 12 % uronic acid was formed.

Example 8: A solution of 30 mmol Cobalt (II) chloride, 60 mmol bipyridine, 450 mg pullulan and 25 mg TEMPO was exposed to oxygen in a closed system.

[0027] A reaction to at least 20% conversion proceeds as follows from the oxygen

consumption (measured with a gas burette; the rate is 3 ml per hour).

Claims

1. A process for producing nitrosonium ions by oxidising a nitroxyl compound with an oxidising agent, *characterised* in that the nitroxyl compound is oxidised in the presence of a complex of a transition metal and a complexing agent.
2. A process according to Claim 1, wherein a the nitroxyl compound is a di-tert-nitroxyl compound, especially 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO).
3. A process according to Claim 1 or 2, wherein the transition metal is manganese, iron, cobalt, nickel, copper or vanadium.
4. A process according to any one of Claims 1-3, wherein the complexing agent is a nitrogen-containing compound.
5. A process according to Claim 4, wherein the complexing agent is a bipyridyl or a triazonane or a (poly)histidine.
6. A process for oxidising a carbohydrate with an oxidising agent in the presence of a nitrosonium ion as a catalyst, *characterised* in that the nitrosonium ion is produced by the process according to any one of Claims 1-5.
7. A process according to Claim 6, wherein the carbohydrate is an α -glucan or fructan or a derivative thereof.
8. A process according to any one of Claims 1-7, wherein a carbonyl-containing carbohydrate containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule is produced.
9. A process according to any one of Claims 1-8, wherein the carbohydrate is a hydroxyalkylated carbohydrate or a glycoside.
10. An oxidised carbohydrate, the carbohydrate being selected from disaccharides, oligosaccharides and polysaccharides of the α -glucan, mannan, galactan, fructan, and chitin types and carbohydrate glycosides, containing at least 1 cyclic monosaccharide chain group carrying a carbaldehyde group per 25 monosaccharide units and per average molecule or a chemical derivative thereof.
11. An oxidised carbohydrate according to Claim 10, containing at least 5 mono-

saccharide units per average molecule.

12. A carbohydrate derivative according to Claim 10 or 11, in which derivative at least a part of the carbaldehyde groups has been converted to a group with the formula -CH=N-R or -CH₂-NHR, wherein R is hydrogen, hydroxyl, amino, or a group R¹, OR¹ or NHR¹, in which R¹ is C₁-C₂₀ alkyl, C₁-C₂₀ acyl, a carbohydrate residue, or group coupled with or capable of coupling with a carbohydrate residue.
13. A carbohydrate derivative according to Claim 10 or 11, in which derivative at least a part of the carbaldehyde groups has been converted to a group with the formula -CH(OR³)-O-CH₂-COOR² or -CH(-O-CH₂-COOR²)₂, in which R² is hydrogen, a metal cation or an optionally substituted ammonium group, and R³ is hydrogen or a direct bond to the oxygen atom of a dehydrogenated hydroxyl group of the carbohydrate.
14. A carbohydrate according to any one of Claims 10-13, further containing carboxyl and/or carboxymethyl groups.

INTERNATIONAL SEARCH REPORT

International Application No

PC NL 00/00118

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C07C239/08 C12P7/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE 37 05 785 A (BASF AG) 1 September 1988 (1988-09-01) the whole document ---	1
A	BOBBITT J M ET AL: "ORGANIC NITROSINIUM SALTS AS OXIDANTS IN ORGANIC CHEMISTRY" HETEROCYCLES, XX, XX, vol. 27, no. 2, 1 January 1988 (1988-01-01), pages 509-533, XP000609709 ISSN: 0385-5414 the whole document --- -/-	1

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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Date of the actual completion of the international search

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International Application No
P 'NL 00/00118

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 07303 A (TNO ;BESEMER ARIE CORNELIS (NL); NOOY ARJAN ERIK JOHAN DE (NL)) 16 March 1995 (1995-03-16) page 3, line 17-22 page 5, line 27-31 table 2 ---	6-9
A	"RÖMPP LEXIKON, 10. AUFLAGE" 1999 , GEORG THIEME VERLAG , STUTTGART XP002139876 ÜBERGANGSMETALLE ---	1
X	NOOY DE A E J ET AL: "HIGHLY SELECTIVE TEMPO MEDIATED OXIDATION OF PRIMARY ALCOHOL GROUPS IN POLYSACCHARIDES" RECUEIL DES TRAVAUX CHIMIQUES DES PAYS-BAS,NL,ELSEVIER SCIENCE PUBLISHERS. AMSTERDAM, vol. 113, no. 3, 1 March 1994 (1994-03-01), pages 165-166, XP000560836 ISSN: 0165-0513 the whole document ---	6-14
X	US 3 632 802 A (BEMILLER JAMES N ET AL) 4 January 1972 (1972-01-04) example 5 claims 1,8 ---	10-14
X	US 5 747 658 A (VEELAERT SARAH ET AL) 5 May 1998 (1998-05-05) example 1 claims 10,11 ---	10-14
A	EP 0 124 439 A (AGRONOMIQUE INST NAT RECH) 7 November 1984 (1984-11-07) the whole document -----	10-14

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-9

Claims 1-5 are directed to a process for preparing nitrosonium ions by oxidation of a nitroxyl compound in the presence of a complex of a transition metal and a complexing agent

Claims 6-9 are directed to the use of the nitrosonium compounds for the oxidation of carbohydrates prepared according to the process of claims 1-5

2. Claims: 10-14

These claims are directed to "oxidised carbohydrates"

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
DE 3705785 A	01-09-1988	DE	3872002 A	23-07-1992
		EP	0282760 A	21-09-1988
		JP	2082808 C	23-08-1996
		JP	7116092 B	13-12-1995
		JP	63233943 A	29-09-1988
		US	5118866 A	02-06-1992
WO 9507303 A	16-03-1995	NL	9301549 A	03-04-1995
US 3632802 A	04-01-1972	NONE		
US 5747658 A	05-05-1998	NL	9301905 A	01-06-1995
		AU	1123595 A	23-05-1995
		CA	2175794 A	11-05-1995
		EP	0726916 A	21-08-1996
		FI	961905 A	03-07-1996
		JP	9500414 T	14-01-1997
		WO	9512619 A	11-05-1995
EP 0124439 A	07-11-1984	FR	2545101 A	02-11-1984
		DE	3461938 D	12-02-1987
		JP	59205949 A	21-11-1984
		US	4672034 A	09-06-1987